PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference BP/G-32576A/SAG/GBG	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/07346	International filing date *(day/month/year)* 08.07.2003	Priority date *(day/month/year)* 09.07.2002
International Patent Classification (IPC) or both national classification and IPC A61K47/00		
Applicant SANDOZ AG et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24.01.2004	16.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Estañol Y Cornella, Telephone No. +49 89 2399-8647

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/07346

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-15 as originally filed

Claims, Numbers

1-23 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-23
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-23
Industrial applicability (IA)	Yes:	Claims	1-23
	No:	Claims	

2. Citations and explanations

see separate sheet

Item V.

Reference is made to the following documents:

D1: EP-A-0 955 062 (GENENTECH INC) 10 November 1999 (1999-11-10)
D2: WO 0103741 A
D3: US-A-5 567 677 (HOEKBY ELVY ET AL) 22 October 1996 (1996-10-22)
D4: US-A-5 096 885 (OESWEIN JAMES Q ET AL) 17 March 1992 (1992-03-17)

None of the cited documents discloses a multi-dosage liquid formulation with a concentration of from about 5 mg/ml to about 100 mg/ml human growth hormone (hGH) and glycine, a buffer, a non-ionic surfactant and a preservative, having a pH of from about 6.1 to about 6.3. Thus, the subject-matter of claim 1 is new over the available prior art (Art. 33(2) PCT).

The problem underlying the present invention may be regarded as how to provide a storage stable liquid farmaceutical composition of high concentrations of hGH.

D3 has solved the same problem by providing liquid formulations of high concentrations of hGH (20IU) comprising glycine, citrate or phosphate buffer and benzyl alcohol as preservative. The difference between the formulations of D3 and those of the present invention is that the later further includes a non-ionic surfactant. The use of a non-ionic surfactant as a stabilizing agent of hGH liquid formulations is known from D1 (poloxamer 188 or 184 - claim 19), from D2 (Pluronic^{R} F-68 in Formulation VI) and from D4 (claims 13-15). Thus, the additon of a non-ionic surfactant as a stabilizing agent in hGH liquid formulations is described in documents D1, D2 or D4 as providing the same advantages as in the present application. The skilled person would therefore regard it as a normal option to include this feature in the formulations of D3 in order to solve the problem posed. The subject-matter of present claims 1 to 23 does not therefore seem to involve an inventive step according to Art. 33(3) PCT.